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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,098	TOYODA ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	mdf

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 11 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/21/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 10/7/2005 in which claims 1-6, 8 and 11 were amended, claim 17 was added and claims 15-16 were cancelled. Claims 1-8, 11 and 17 are pending in the instant application.

Any rejection of record in the previous office action mailed on 4/7/2005 not addressed herein is withdrawn. This action is not final due to new grounds of rejection presented herein that were not necessitated by Applicant's amendment of the claims in the response filed 10/7/2005.

Specification

Receipt is acknowledged of the amendment to the specification deleting the phrase "the disclosure of all of which are incorporated herein by reference." The amendment has been found remedial and the objection to the specification is hereby withdrawn.

Claim Objections

Claim 8 is objected to because of the following informalities: claim 8 recites a "UDP-2" promoter in line 5 and

should recite a "UCP-2" promoter. Appropriate correction is required.

Claims 2-4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Regarding claims 2 and 3, the PPRE and C/EBP binding sequence recited in these claims are not limited to their respective nucleotide sequences recited in claim 1, upon which they are dependent.

Regarding claim 4, the isolated DNA described in claim 1 is not further limited by recitation of "wherein the part of said base sequence is a base sequence presented by position 255 to 430 of SEQ ID NO: 1, position 255 to 717 of SEQ ID NO: 1, position 717 to 1133 of SEQ ID NO: 1, position 1133 to 1389 of SEQ ID NO: 1, position 255 to 1857 of SEQ ID NO: 1, position 571 to 2270 of SEQ ID NO: 1, position 717 to 2270 of SEQ ID NO: 1, position 1133 to 2270 of SEQ ID NO: 1 position 1389 to 2270 of SEQ ID NO: 1, or position 1634 to 2270 of SEQ ID NO: 1." For example, position 1133 to 1389 of SEQ ID NO: 1 encompasses all

of the C/EBP sequence (nucleotides 1364 to 1368 of SEQ ID NO: 1) listed in claim 1(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 11, and therefore dependent claims 5-8 and 17, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following are new rejections.

Claim 1 recites "an uncoupling protein-2 (UCP-2) promoter region, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of:

a. a perixosome proliferators response element (PPRE) sequence comprising nucleotides 284-296 of SEQ ID NO: 1;

b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides

1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;

c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1." Claim 1 is vague and indefinite in that the metes and bounds of "or part" are unclear: does Applicant intend for the UCP-2 promoter region to encompass *a single* part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from a-d; or does the claim encompass discontiguous parts as long as one part meets the rest of the claim limitations? The indefinite nature of the first reference to "part" in claim one makes the antecedent basis of "the part" recited in line 4 improper.

Claim 2 recites "[t]he isolated DNA described in claim 1 wherein the regulator sequence comprises a peroxisome proliferator response element (PPRE)" in lines 1-2. Claim 2 is vague and indefinite in that it is unclear whether Applicant intends the PPRE of claim 1 or any PPRE.

Claim 3 recites "[t]he isolated DNA described in claim 1 wherein the regulator sequence comprises a CCAAT/enhancer binding protein (C/EBP) binding sequence" in lines 1-2. Claim 3 is vague and indefinite in that it is unclear whether Applicant intends the C/EBP binding sequence of claim 1 or any C/EBP binding sequence.

Claim 4 recites "[t]he isolated DNA described in claim 1 wherein the part of said base sequence is a base sequence presented by position 255 to 430 of SEQ ID NO: 1…" in lines 1-4. Claim 4 is vague and indefinite in that it is unclear what is meant by "presented." Is this "closed" language (e.g. consisting of), "open language" (e.g. comprising of) or neither?

Claim 11 recites "a UCP-2 promoter activity, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, which the part of the base sequence comprises a regulator sequence selected from the group consisting of:

a. a perixosome proliferators response element (PPRE) sequence comprising nucleotides 284-296 of SEQ ID NO: 1;

b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;

c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1" in lines 8-24. Claim 11 is vague and indefinite in that the metes and bounds of "or part" are unclear as described above for claim 1. Also, as recited above, the indefinite nature of the first reference to "part" in claim 11 makes the antecedent basis of "the part" recited in line 11 improper.

Response to Arguments

As all of the above rejections are new rejections, Applicant's arguments with regard to the previously cited rejections are rendered moot.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 11, and therefore dependent claim 17, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection based upon the grounds that there is insufficient description of the broad genus of nucleic acids encompassed by the term "UCP-2 promoter" and the corresponding "UCP-2 promoter activity" to reasonably convey to the skilled artisan that Applicant had possession of the broadly claimed invention at the time of filing.**

Claims 8 and 11 recite a "UCP-2 promoter" as well as "UPC-2 promoter activity" and are directed to the DNA described in claim 1: an uncoupling protein-2 (UCP-2) promoter region, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of:

a. a perixosome proliferators response element (PPRE) sequence comprising nucleotides 284-296 of SEQ ID NO: 1;

b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;

c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1.

The claims do not provide any structural information with regard to what is encompassed by a UCP-2 promoter. Thus, the rejected claims comprise a set of nucleic acid sequences that are defined by their activity.

To provide adequate written description and evidence of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof.

Other than to say that the "UCP-2 promoter was found in the 3.3 kb DNA of the upstream region of the human UCP-2 structural

gene," no information is provided in the specification regarding the boundaries for what is considered a UCP-2 promoter. Moreover, there is no limitation in the rejected claim that the cited terms are limited to the human UCP-2 promoter, even if such boundaries were clearly defined in the instant specification for the human promoter region. While claim 1 recites that the promoter region comprises nucleotides 1-2270 of SEQ ID NO: 1, it also encompasses embodiments that are just part of SEQ ID NO: 1 as long as the part includes a regulator sequence selected from the recited PPRE, C/EPB, GRE and Myo-D binding sequences. Thus, the rejected claims read on an extremely large number of different nucleic acid sequences.

The instant specification is directed to the characterization of the ~2.3 kb hUCP-2 promoter region described by SEQ ID NO: 1 from nucleotides 1-2270. Very short sequences within this fragment were identified as well-known binding sites for different transcription regulators (e.g. the specifically recited oligonucleotide sequences recited in claim 1). Deletion constructs comprising portions of this region were made and the reporter gene activity determined (e.g. see Figure 9 and Example 4 at pages 25-26 of the instant specification). An ~70% increase in UCP-2 promoter region activity was observed upon loss of the PPRE element at nucleotides 284-296 of SEQ ID NO: 1.

When the two C/EBP binding sites were deleted, about 30% of the UCP-2 promoter region activity was lost, suggesting these sequences were enhancers of UCP-2 promoter region activity. Thus, the instant specification does provide some data with regard to the basis organization and functional charactestics of the human UCP-2 promoter region described by nucleotides 1-2270 of SEQ ID NO: 1. However, there is no basis provided by the instant specification for one of skill in the art to envision what other sequences upstream from the described region might play a role in UCP-2 expression. Furthermore, no basis is provided by the instant specification for the skilled artisan to extrapolate these findings to species other than humans (e.g. whale, mouse, horse, etc.)

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of UPC-2 promoter nucleotide sequences. For example, the prior art does not appear to have taught that the specifically recited regulatory elements of claim 1 were known to be associated with any other known UCP-2 promoter sequence (e.g. murine).

Given the large genus of UCP-2 promoters encompassed by the rejected claims and the lack of any basis in the prior art or instant specification to envision other UCP-2 promoters encompassed by the claims, the skilled artisan would not have

been able to envision a sufficient number of specific embodiments of such UCP-2 sequences so as to describe the broadly claimed genus of such promoters. Therefore, one skilled in the art would reasonably have concluded that Applicant was not in possession of the broadly claimed invention.

Response to Arguments

Although this is a new rejection, it is quite similar in nature to that set forth in the office action of 4/7/2005. Thus, although Applicant's arguments are technically rendered moot, for the purposes of expedited prosecution Applicant's arguments are addressed below to the extent that they pertain to the new rejection above.

Applicant argues in the papers filed 10/7/2005 that the specification discloses seven deletion mutants in which one or more regulator sequences were deleted and that in six mutants promoter activity was maintained to varying degrees. Applicant further argues that the UCP-2 promoter of the present invention can be utilized as a tool for screening a compound that regulates expression of UCP-2 by acting on any element in the regulatory region. Furthermore, Applicant argues that one of skill in the art can easily prepare, and use, any fragment containing a target regulator sequence. Finally, Applicant

submits that it is possible to screen an agent for regulating an expression of UCP-2 in non-human, as well as human, animals using the human promoter sequence.

These arguments do not address the structure and/or function of a UPC-2 promoter, the distinguishing identifying characteristics of a UPC promoter, the chemical properties of a UPC-2 promoter or any combination of the above as opposed to the disclosed human UPC-2 promoter region which comprises the regulatory sequences set forth in claim 1. Utilization of a one nucleotide sequence (or specific regulatory elements from that sequence) for screening does not impart possession of a broad genus of UPC-2 promoters.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Surwit et al (WO 98/31396, of record). **This rejection is maintained for reasons of record and slightly**

altered to take into consideration Applicant's amendment in the papers filed 10/7/2005.

Applicant's invention is drawn to a UCP-2 promoter region which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of

a. a perixosome proliferators response element (PPRE) sequence comprising nucleotides 284-296 of SEQ ID NO: 1;

b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;

c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1. Applicant's invention is further drawn to the isolated DNA described in claim 1 wherein the regulator sequence comprises a PPRE element and wherein the regulator sequence comprises a C/EBP binding sequence (claims 2-3). Applicant's invention is further drawn to the isolated DNA of

claim 1 wherein the part of said base sequence is a base sequence presented by position 255 to 430 of SEQ ID NO: 1, position 255 to 717 of SEQ ID NO: 1, position 717 to 1133 of SEQ ID NO: 1, position 1133 to 1389 of SEQ ID NO: 1, position 255 to 1857 of SEQ ID NO: 1, position 571 to 2270 of SEQ ID NO: 1, position 717 to 2270 of SEQ ID NO: 1, position 1133 to 2270 of SEQ ID NO: 1, position 1389 to 2270 of SEQ ID NO: 1, or position 1634 to 2270 of SEQ ID NO: 1. Applicant's invention is further drawn to a recombinant vector comprising the DNA of claim 1 (claim 5) and said recombinant vector which comprises a DNA comprising a structural gene under the control of the UCP-2 promoter region comprising the regulator sequence (claim 6) as well as a tranformant transformed by the recombinant vector described in claim 5 (claim 7). Applicant's invention is further drawn to a method for screening for a compound or its salt that promotes or inhibits a UCP-2 promoter activity which comprises measuring the expression level of the structural gene in the transformant of claim 7 contacted to a compound or its salt and that in a control transformant, with no UCP-2 promoter, contacted to a second sample of the compound or its salt, and comparing the expression levels thereof.

The Surwit et al application teaches the identification and cloning of nucleic acid sequences encoding human uncoupling

protein 2 (hUCP-2), 5' sequences controlling the expression of hUCP-2 expression, as well as methods of using the regulator sequences to identify modulators of hUCP-2 expression. For example, the application teaches the identification of a human BAC clone comprising approximately 20 kb of human sequence which the practitioners believe comprises the entire gene and entire promoter (hUCP2.BAC deposited with the ATCC; e.g. see page 16-17). Further, the application teaches the isolation of a lambda EMBL3 phage comprising ~14 kb of human sequences. This clone comprises all 8 exons of the human UCP-2 gene, as well as a minimum of 3 kb of DNA upstream of the putative +1 site (e.g. page 32). The application teaches methods of screening compounds for their ability to modulate (e.g. increase or inhibit) the activity or expression of UCP-2. Such methods can be performed *in vivo* or *in vitro* using cells expressing the human UCP-2 gene (or cells expressing a reporter sequence operatively linked to the UCP-2 regulatory sequences) that are incubated in the presence and absence of test compounds and the level of expression in each case determined (e.g. page 19, lines 2-18).

Given the size of the genomic clones obtained by the inventors of the Surwit et al application (e.g. at least 3 kb upstream of the transcription initiation site) and the fact that

the sequences recited in the claims are all within ~2.2 kb of the initiation site (e.g. see amended Figure 4 of the instant specification), it is reasonable to expect that the clones obtained by Surwit et al necessarily comprise at least the specific regulator sequences recited in rejected claims 1-8.

Response to Arguments

Applicants traverse the anticipation rejection and maintain their arguments of record which have been fully considered but are respectfully found unpersuasive. Applicant specifically argues that **1)** the instant specification discloses regulator sequences and experimental data regarding the isolated DNA of claim 1, including deletion mutants **2)** Surwit only discloses a partial sequence listing and at least part of the disclosed sequence is at variance with SEQ ID NO: 1 disclosed by Applicant **3)** Surwit does not disclose the sequence where the regulator sequences specified in claim 1 would be located **4)** Surwit does not include a sequence listing and therefore the sequences recited in claim 1 are not clearly included in the disclosure of Surwit **5)** it is impossible to consider the undisclosed sequence between Sequence 1 and Sequence 2 of Surwit and the Patent Office has not established a prima facie anticipation or obviousness of these sequences and their respective

classifications by Surwit **6)** requiring Applicant to obtain one or more cell lines of Surwit and then to isolate, clone and sequence the DNA in order to compare it with Applicant's DNA is unduly burdensome **7)** if, as indicated on the cover sheet of the PCT application, Surwit et al have since filed either a national phase application under 35 U.S.C. §371 or a *bona fide* continuation or divisional, the Patent Office should have required submission of an electronic copy of the sequence listing of Surwit and would therefore be in the best position to compare the two sequences **8)** Applicant has compared the sequence of the instant application with that disclosed in Figures 10B and 10C of Surwit et al and have attached the sequence alignment comparison (Exhibit A). Applicant notes that the sequence consisting of nucleotides 2328 to 2357 of SEQ ID NO: 1 of the instant application is deleted in Surwit and contend that if this deletion has occurred, there is a "high probability of deletion of the regulator sequence in the Surwit clone" (page 23 of the papers filed 10/7/2005).

The first seven arguments are of record and Examiner's response is maintained and slightly altered in order to take into consideration Applicant's amendment. The rejected claims are directed to a nucleic acid that comprises a UCP-2 promoter region which comprises all or part of the base sequence

consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from a group of well known transcription factor/enhancer binding sequences. Thus the claims encompass any UCP-promoter region sequence that includes as few as five nucleotides (e.g., the CCAAT/enhancer binding protein sequence of nucleotides 1316 to 1320 of SEQ ID NO: 1). These regulator binding sequences are well known and highly conserved as has already been established in the record. It is Examiner's contention that, based on the reasons above, Surwit et al anticipates at least the claimed regulator sequences which, without exception, are located 5' to any discrepancies noted by the comparison of the partial sequence disclosure of Surwit et al and nucleotides 1733 to 2270 of Applicant's SEQ ID NO: 1 in Exhibit A. Deletions of nucleotides outside the claimed sequence boundaries are not relevant to an anticipation rejection. Moreover, Applicant admits that "the deletion may be due to a cloning artifact, rather than to a deletion from the genome" (page 23 of the papers file 10/7/2005). Furthermore, there is reason to expect that while there might be variance in the broad region of the nucleic acid sequence not explicitly disclosed by Surwit et al from Applicant's own data, this variance is unlikely to extend into the specifically recited

regulator sequences described by Applicant. These sites are very short sequences that are extraordinarily well conserved across multiple different genes obtained from many different animal species as evidenced by Exibits A-H of the previous office action. Furthermore, Applicant's own data suggests that these regulator sequences are important to UCP-2 gene regulation and are, therefore, even more likely to be conserved. It is exceedingly unlikely, given the facts outlined above and this conservation in sequence across species for many very different genes, that the specifically recited enhancer sites are not present in the clones disclosed by Survit et al. Thus, one of skill in the art would necessarily expect that the deposited material would meet the structural/functional limitations for the UCP-2 promoter region sequences of the rejected claims.

The teachings of Surwit et al are also disclosed in U.S. 2003/0119775 A1. The US application does not appear to comprise a sequence listing that discloses the relevant sequences so that the Examiner could do the comparison for Applicant. However, arguments directed to an undue burden placed upon Applicant in this regard are irrelevant. Applicant's response has not effectively rebutted Examiner's argument that one would necessarily expect the clones disclosed by Surwit et al to possess the recited structural and functional characteristics.

As indicated in the record, the Office does not have the facilities for examining and comparing an applicant's claimed product with the products of the prior art, and the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application

Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter A. Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM. A phone message left at

this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office.)

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

December 16, 2005

JAMES KETTER
PRIMARY EXAMINER